Is JYNARQUE® (tolvaptan) right for your adult patients with ADPKD?

A guide for identifying patients who may be appropriate for JYNARQUE

ADPKD=autosomal dominant polycystic kidney disease.

INDICATION:

JYNARQUE is indicated to slow kidney function decline in adults at risk of rapidly progressing autosomal dominant polycystic kidney disease (ADPKD).

WARNING: RISK OF SERIOUS LIVER INJURY

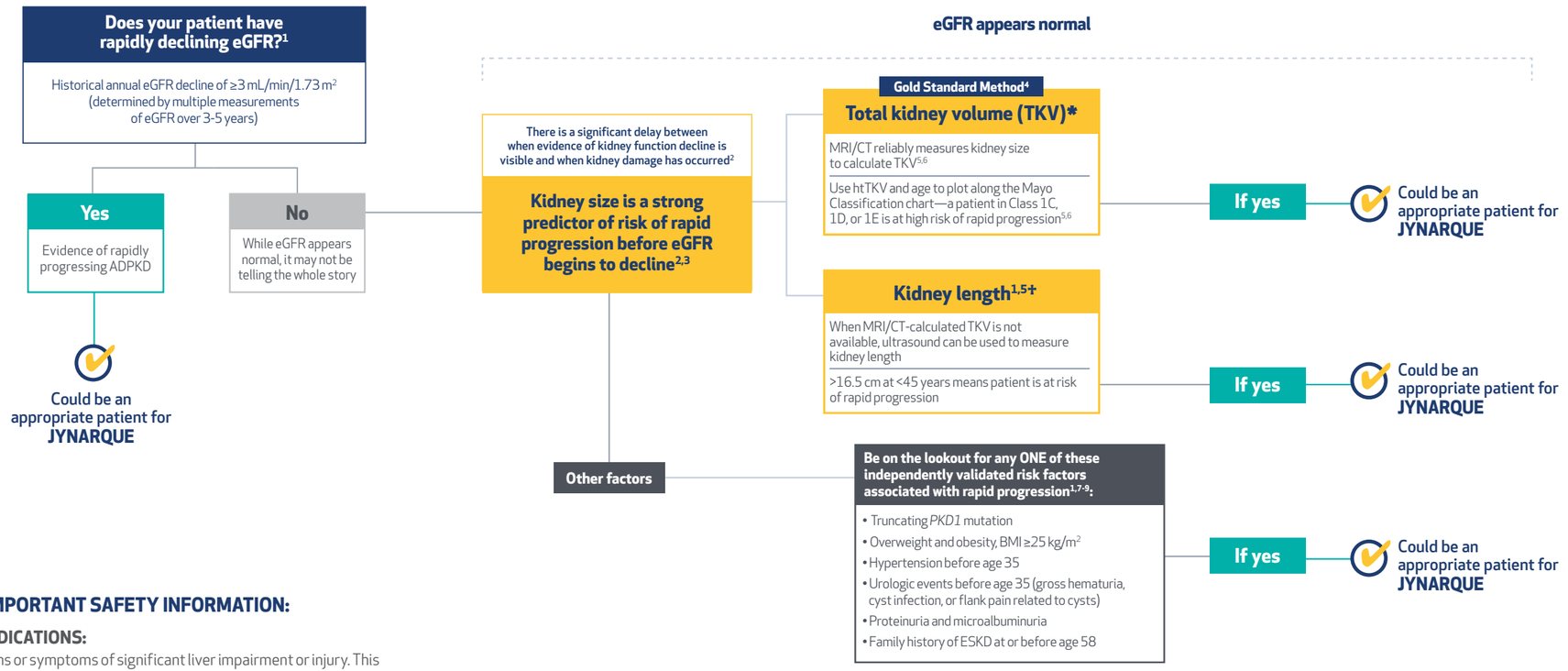
- **JYNARQUE® (tolvaptan) can cause serious and potentially fatal liver injury. Acute liver failure requiring liver transplantation has been reported**
- **Measure transaminases (ALT, AST) and bilirubin before initiating treatment, at 2 weeks and 4 weeks after initiation, then monthly for the first 18 months and every 3 months thereafter. Prompt action in response to laboratory abnormalities, signs, or symptoms indicative of hepatic injury can mitigate, but not eliminate, the risk of serious hepatotoxicity**
- **Because of the risks of serious liver injury, JYNARQUE is available only through a Risk Evaluation and Mitigation Strategy program called the Tolvaptan for ADPKD Shared System REMS**

Please see **IMPORTANT SAFETY INFORMATION** on the second page.

JYNARQUE® (tolvaptan)
15, 30, 45, 60, 90 mg tablets

Once you've confirmed a patient's ADPKD diagnosis

Taking a holistic assessment can identify appropriate patients for JYNARQUE® (tolvaptan)



SELECT IMPORTANT SAFETY INFORMATION:

CONTRAINDICATIONS:

- History, signs or symptoms of significant liver impairment or injury. This contraindication does not apply to uncomplicated polycystic liver disease
- Taking strong CYP3A inhibitors
- With uncorrected abnormal blood sodium concentrations
- Unable to sense or respond to thirst
- Hypovolemia
- Hypersensitivity (e.g., anaphylaxis, rash) to JYNARQUE or any component of the product
- Uncorrected urinary outflow obstruction
- Anuria

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BMI=body mass index; CKD=chronic kidney disease; CT=computed tomography; eGFR=estimated glomerular filtration rate; ESKD=end-stage kidney disease; htTKV=height-adjusted total kidney volume; MRI=magnetic resonance imaging.

*Identifying a TKV greater than expected for your patient's age can provide an early and reliable marker for rapid disease progression in ADPKD.[10,11]

†A kidney length of >16.5 cm was shown to predict development of CKD Stage 3 within 8 years in patients with ADPKD who were <45 years of age and who had CKD Stage 1 or 2.[3]

Physician should use their clinical judgment when assessing each patient for treatment with JYNARQUE.

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Otsuka is committed to making JYNARQUE® (tolvaptan) affordable and available

Eligible commercially insured patients pay as little as **$10** per month for JYNARQUE.*

>83% of patients with commercial insurance have coverage for JYNARQUE.[16]

*Assumes one 28-day supply prescription per month. If more than one prescription is filled in a calendar month, patient may pay more than $10 in that month. Offer is not transferable. Patients are not eligible if they are under 18 years of age, or are covered in whole or in part by any state program or federal healthcare program, including but not limited to, Medicare or Medicaid (including Medicaid managed care), Medigap, VA, DOD, or TRICARE. Only valid in US and Puerto Rico. Offer void where prohibited by law, taxed or restricted. Other restrictions may apply. This program is not health insurance. Otsuka America Pharmaceutical, Inc. has the right to rescind, revoke or amend this program at any time without notice. Your participation in this program confirms that this offer is consistent with your insurance coverage and that you will report the value received if required by your insurance provider. When you use this program, you are certifying that you understand and comply with the program rules, terms and conditions.

References: 1. Kidney Disease: Improving Global Outcomes (KDIGO) Work Group. *Kidney Int*. 2025;107(suppl 2S):S1-S239. **2.** Grantham JJ, Mulamalla S, Swenson-Fields KI. *Nat Rev Nephrol*. 2011;7(10):556-566. **3.** Bhutani H, Smith V, Rahbari-Oskoui F, et al; for the CRISP Investigators. *Kidney Int*. 2015;88(1):146-151. **4.** Zhang W, Blumenfeld JD, Prince MR. *J Magn Reson Imaging*. 2019;50(1):41-51. **5.** Magistroni R, Corsi C, Martí T, Torra R. *Am J Nephrol*. 2018;48:67-78. **6.** Irazabal MV, Rangel LJ, Bergstralh EJ, et al. *J Am Soc Nephrol*. 2015;26(1):160-172. **7.** Rastogi A, Ameen KM, Al-Baghdadi M, et al. *Ther Clin Risk Manag*. 2019;15:1041-1052. **8.** Nowak K, You Z, Gitomer B, et al. *J Am Soc Nephrol*. 2018;29(2):571-578. **9.** Cornec-Le Gall E, Audrézet MP, Rousseau A, et al. *J Am Soc Nephrol*. 2016;27(3):942-951. **10.** Chapman AB, Bost JE, Torres VE, et al. *Clin J Am Soc Nephrol*. 2012;7(3):479-486. **11.** Yu ASL, Shen C, Landsittel DP, et al. *Kidney Int*. 2018;93(3):691-699. **12.** Data on file. TOLV-008. Otsuka America Pharmaceutical, Inc.; Rockville, MD. **13.** Torres VE, Chapman AB, Devuyst O, et al; for the TEMPO 3:4 Trial Investigators. *N Engl J Med*. 2012;367(25):2407-2418. **14.** Torres VE, Chapman AB, Devuyst O, et al; for the REPRISE Trial Investigators. *N Engl J Med*. 2017;377(20):1930-1942. **15.** Otsuka proprietary data. REF-20244. Otsuka America Pharmaceutical, Inc.; Rockville, MD. **16.** Managed Markets Insight & Technology, LLC database as of July 2023.

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INDICATION and IMPORTANT SAFETY INFORMATION for JYNARQUE® (tolvaptan)

INDICATION:

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IMPORTANT SAFETY INFORMATION:

WARNING: RISK OF SERIOUS LIVER INJURY

- **JYNARQUE® (tolvaptan) can cause serious and potentially fatal liver injury. Acute liver failure requiring liver transplantation has been reported**
- **Measure transaminases (ALT, AST) and bilirubin before initiating treatment, at 2 weeks and 4 weeks after initiation, then monthly for the first 18 months and every 3 months thereafter. Prompt action in response to laboratory abnormalities, signs, or symptoms indicative of hepatic injury can mitigate, but not eliminate, the risk of serious hepatotoxicity**
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CONTRAINDICATIONS:

- History, signs or symptoms of significant liver impairment or injury. This contraindication does not apply to uncomplicated polycystic liver disease
- Taking strong CYP3A inhibitors
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- Anuria

Serious Liver Injury: JYNARQUE can cause serious and potentially fatal liver injury. Acute liver failure requiring liver transplantation has been reported in the post-marketing ADPKD experience. Discontinuation in response to laboratory abnormalities or signs or symptoms of liver injury (such as fatigue, anorexia, nausea, right upper abdominal discomfort, vomiting, fever, rash, pruritus, icterus, dark urine or jaundice) can reduce the risk of severe hepatotoxicity. To reduce the risk of significant or irreversible liver injury, assess ALT, AST and bilirubin prior to initiating JYNARQUE, at 2 weeks and 4 weeks after initiation, then monthly for 18 months and every 3 months thereafter.

Hypernatremia, Dehydration and Hypovolemia: JYNARQUE therapy increases free water clearance which can lead to dehydration, hypovolemia and hypernatremia. Instruct patients to drink water when thirsty, and throughout the day and night if awake. Monitor for weight loss, tachycardia and hypotension because they may signal dehydration. Ensure abnormalities in sodium concentrations are corrected before initiating therapy. If serum sodium increases above normal or the patient becomes hypovolemic or dehydrated and fluid intake cannot be increased, suspend JYNARQUE until serum sodium, hydration status and volume status parameters are within the normal range.

Inhibitors of CYP3A: Concomitant use of JYNARQUE with drugs that are moderate or strong CYP3A inhibitors (e.g., ketoconazole, itraconazole, lopinavir/ritonavir, indinavir/ritonavir, ritonavir, and conivaptan) increases tolvaptan exposure. Use with strong CYP3A inhibitors is contraindicated; dose reduction of JYNARQUE is recommended for patients taking moderate CYP3A inhibitors. Patients should avoid grapefruit juice beverages while taking JYNARQUE.

Adverse Reactions: Most common observed adverse reactions with JYNARQUE (incidence >10% and at least twice that for placebo) were thirst, polyuria, nocturia, pollakiuria and polydipsia.

Other Drug Interactions:

- **Strong CYP3A Inducers:** Co-administration with strong CYP3A inducers reduces exposure to JYNARQUE. Avoid concomitant use of JYNARQUE with strong CYP3A inducers
- **V_2-Receptor Agonist:** Tolvaptan interferes with the V_2-agonist activity of desmopressin (dDAVP). Avoid concomitant use of JYNARQUE with a V_2-agonist

Pregnancy and Lactation: Based on animal data, JYNARQUE may cause fetal harm. In general, JYNARQUE should be discontinued during pregnancy. Advise women not to breastfeed during treatment with JYNARQUE.

To report SUSPECTED ADVERSE REACTIONS, contact Otsuka America Pharmaceutical, Inc. at 1-800-438-9927 or FDA at 1-800-FDA-1088 (www.fda.gov/medwatch).

Please read FULL PRESCRIBING INFORMATION, including **BOXED WARNING**.

JYNARQUE® (tolvaptan) is indicated for adults at risk of rapidly progressing ADPKD

- **Studied in the 2 largest clinical trials of patients with ADPKD across CKD stages 1-4[12-14]**
- **Prescribed by over 5,500 physicians to more than 10000 patients with rapidly progressing ADPKD[15]**

Learn how you can change the course for your patients with ADPKD

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